Poster Session II

BIOMEDICAL IMPLICATIONS OF OXYGEN RADICALS

OXYGEN RADICALS IN THE PATHOGENESIS OF EDEMA

A. C. Allison, R. Alvarez, C. W. Laughton and A. J. Tomolonis, Institute of Biological Sciences, Syntex Research, 3401 Hillview Avenue, Palo Alto, CA 94304.

Edema in the lung and other tissues can be induced by agents generating oxygen radicals. Exposure of cultured endothelial cells to xanthine oxidase or t-butylhydroperoxide causes reversible retraction, which in vivo could allow exudation of plasma. The role in this process of oxygen-radical-mediated activation of guanylate cyclase and cyclic AMP phosphodiesterase will be discussed.

Oxy-Radical Production and Cardiotoxicity of Anthracyclines Catalyzed By Mitochondrial NADH Dehydrogenase

Kelvin J.A. Davies, Department of Physiology and Biophysics, Harvard Medical School, 25 Shattuck St., Bldg. C1, Boston, Mass. 02115.

The anthracyclines adriamycin and daunorubicin are effective chemotheraputic (anti-cancer) agents whose use is limited by damage to normal cells: Particularly cardiotoxicity. Our results demonstrate that cardiac mitochondrial NADH dehydrogenase mediates a one-electron reduction of adriamycin and daunorubicin to reactive free radicals. The subsequent dismutation of these anthracycline radicals initiates an oxy-radical cascade which, ultimately, results in cellular damage. A new anthracycline derivative, 5-iminodaunorubicin, was found to be essentially unreactive towards NADH dehydrogenase (causing little or no drug, or oxygen radical production), yet demonstrates anti-tumor activity in vitro. Thus, 5-iminodaunorubicin may prove to be an effective anti-cancer agent, devoid of cardiotoxic side effects.

LYTIC EFFECTS OF O_2 RADICALS ON RESEALED RBC GHOSTS.

A. W. Girotti and J.P. Thomas Department of Biochemistry, The Medical College of Wisconsin, Milwaukee, WI 53226

Resealed erythrocyte (RBC) ghosts containing Na^+ and glucose-6-P (G6P) as markers lyse when exposed to the xanthine/xanthine oxidase/iron system. In the absence of EDTA, marker release accelerates after a lag, Na^+ preceding G6P. Efflux and accompanying thiobarbituric acid-detectable lipid peroxidation (LP) can be totally inhibited by superoxide dismutase (SOD) or catalase (CAT). In the presence of EDTA (2-fold over iron) LP and G6P efflux are reduced to background levels while Na^+ efflux is first order and $\sim$ 3-fold over background. The latter effect is totally inhibited by CAT, but minimally by SOD. These results suggest that different membrane targets responsible for Na^+ and G6P release have been resolved.